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#37 Appeal Brief (3) 5/9/96

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Before the Board of Patent Appeals and Interferences

In re PATENT APPLICATION OF

WEINBERG et al

Atty. Ref.: 1579-21

Serial No.: 08/047,068

Group Art Unit: 1816

Filed: April 16, 1993

Examiner: Gambel, P.

For: A METHOD OF INHIBITING HIV INFECTION

* * * * *

April 22, 1996

APPEAL BRIEF

Hon. Commissioner of Patents
and Trademarks
Washington, DC 20231

Sir:

This is an appeal from the final rejection of claims 8, 9, 11 and 13-19. No claim stands allowed.

REAL PARTY IN INTEREST

The real party in interest in this application is Duke University of Durham, North Carolina.

RELATED APPEALS AND INTERFERENCES

No other appeals or interferences are known to Appellants, Appellants' legal representative, or assignee which will directly affect or be directed affected by or have a bearing on the Board's decision in the pending appeal.

STATUS OF THE CLAIMS

Claims 8, 9, 11 and 13-19 are pending in this application and have been finally rejected. Claims 1-7 were cancelled in the Amendment filed December 23, 1993. Claims 10 and 12 stand withdrawn from consideration. The claims on appeal are set forth in the attached Appendix.

STATUS OF THE AMENDMENTS

The claim revisions proposed in the Amendment under Rule 116 filed December 18, 1995, have not been entered.

SUMMARY OF THE INVENTION

In one embodiment, the present invention relates to a method of inhibiting HIV infection of cells susceptible to HIV infection. The method comprises contacting the cells with an amount of an agent that inhibits CD44-facilitated entry of HIV into the cells sufficient to effect the inhibition. (See claim 8 and claim a depending therefrom.)

In a specific embodiment, the present invention relates to a method of inhibiting CD44-facilitated HIV infection of a cell susceptible to HIV infection. The method comprising contacting the cell with an amount of an anti-CD44 antibody sufficient bind to CD44 molecules present on the surface of the cell and thereby inhibit the CD44-facilitated infection of the cell. (See claim 16 and claims depending therefrom.)

Support for the invention as claimed in claims 8, 9, 11 and 13-19 can be found, for example, at pages 29-30 and in the working Example at page 31.

The foregoing represents a concise summary of the invention.

THE ISSUES

Claims 8, 9, 11 anc 13-19 stand rejected under 35 USC 112, first paragraph, as the subject specification allegedly fails to provide an adequate written description of the invention and allegedly fails to teach how to make and/or use the invention.

Claim 11 stands rejected under 35 USC 112, first paragraph, as it is allegedly unclear as to whether the claimed biological materials are (1) known and readily available to the public, (2) sequenced, or (3) deposited.

Claim 11 also stands rejected under 35 USC 112, second paragraph.

Claims 17 and 19 stand rejected under 35 USC 112, first paragraph, as the specification allegedly fails to provide an adequate written description of the invention.

Accordingly, the issues presented for review are:

i) whether the subject matter of claims 8, 9, 11 and 13-19 is enabled by the disclosure;

ii) whether the subject matter of claim 11 is enabled by the disclosure;

iii) whether claim 11 is definite; and

iv) whether the subject matter claims 17 and 19 is supported by the disclosure.

GROUPING OF THE CLAIMS

For each ground of rejection that applies to two or more claims, those claims do not stand or fall together for the reasons that follow.

THE ARGUMENTS

i) Rejection of claims 8, 9, 11 and 13-19 under 35 USC 112, first paragraph.

The Examiner's rejection of the claims as non-enabled is in error for the reasons that follow.

The Examiner contends that Appellants have not disclosed how to use CD44-specific antibodies therapeutically in mammals. The Examiner comments on an alleged lack of correlation between *in vitro* and *in vivo* operability of the claimed therapeutic

strategy. The Examiner further states that, in the area to which the invention relates, *in vitro* and animal studies have not correlated well with clinical trial results in humans.

The Examiner's comments in support of the rejection would appear to relate more properly to a rejection under 35 USC 101 than 35 USC 112. Such a rejection was made in this case, but was subsequently withdrawn. Accordingly, the record indicates that the question of utility has been adequately addressed and comments relating, for example, to correlations between models and humans and the "asserted operability" of the claimed invention are submitted to be improper.

The subject specification teaches how to make and how to use the invention. It fully discloses how to make the anti-CD44 antibodies and how to use those antibodies to inhibit infection of cellular targets. Mononuclear phagocytes, which are concentrated in the mucosa, are a particularly important target and cells of this type are specifically recited in claim 13 and claims depending therefrom and in claim 19.

One skilled in the art would appreciate that for *in vivo* treatment, intravenous administration is appropriate. For *ex*

vivo use, to which claim 19 is specifically directed and which is described at page 30 of application, last paragraph, the agent can simply be mixed with a potentially infected product (eg blood, blood plasma, or purified blood factor) before administration of that product to the patient. *Ex vivo* mixing would prevent infection of host cells by the administered product. For topical treatment, to which claim 18 is specifically directed, the agent can be administered in a solution (eg liquid or gel or foam form) within a condom or to a mucosal surface. In this regard, page 30 of application, lines 20-22, are noted. So administered, HIV infection of the mononuclear phagocytes (eg on mucosal surfaces) can be inhibited.

Optimum formulations and dosing regimens to be used can be readily established by one skilled in the art - no undue experimentation would be required. Indeed, the Examiner has not indicated why such would not be the case.

As indicated above, claims 13 and 19 relate to inhibition of HIV infection of mononuclear phagocytes (claim 14 specifically recites human monocytes). The manuscript of Rivadenevia (of record) makes clear the inhibition of HIV infection of

mononuclear phagocytes and indeed the Examiner has acknowledged the positive results presented therein. The Examiner appears to fault the document for not showing 100% effectiveness using the CD44-specific antibodies. Such levels are not required to satisfy the requirements of 35 USC 112. Indeed, many commercially important drugs are not 100% effective.

Summarizing, the subject specifically teaches how to make and how to use the subject matter of each of the claims on appeal. Claims 13 (and claims depending therefrom) and 19 recite mononuclear phagocytes which are of particular importance in HIV transmission. Claim 17 is limited to mononuclear phagocytes concentrated at the mucosa which is a readily accessible body surface. Claim 18 is limited to topical administration which is particularly well suited for such cells. The concerns expressed by the Examiner are submitted to be particularly inapplicable to the subject matter of these dependent claims.

Reversal is requested.

ii) Rejection of claim 11 under 35 USC 112, first paragraph.

The Examiner's rejection of claim 11 under 35 USC 112, first paragraph, is in error and should be reversed for the reasons that follow.

The Examiner contends that evidence of availability to the public of the A1G3 antibody/hybridoma is not of record. On the contrary, it was pointed out in the December 18, 1995 Amendment that A1G3 has been publicly available since prior to April 1991. Documentation from the American Type Culture Collection (ATCC) making clear the contribution of A1G3 to the Collection on December 16, 1988, was submitted by Supplemental Amendment under Rule 116 on December 19, 1995. This document evidences the public availability of the A1G3. Nothing more should be required.

Reversal is requested.

iii) Rejection of claim 11 under 35 USC 112, second paragraph.

The Examiner's rejection of claim 11 as indefinite is not well founded. A1G3 has specific meaning as evidenced by the ATCC documentation referred to in paragraph (ii) above. The subject

specification defines A1G3 as an anti-CD44 antibody (see page 31, line 17) and the ATCC "Collection of Animal Cell Lines" form dated December 16, 1988 (giving A1G3 ATCC No. HB177) provides the source and characteristics of the cell line. Further, the ATCC form makes reference to pertinent publications.

In view of the above, it should be clear that A1G3 is not merely "a laboratory designation". Rather, A1G3 has clear meaning to those skilled in the art who have long had access via the ATCC.

Reversal is requested.

iv) Rejection of claims 17 and 19 under 35 USC 112, first paragraph.

Submitted concurrently herewith is an Amendment under Rule 116 which revises claim 17 to make the language used more consistent with that of the disclosure at page 30, line 22. The Amendment revises claim 19 so as to replace the term "*ex vivo*" with "*in vitro*" which is fully supported by the disclosure. Entry of the proposed claim revisions is requested. Should that Amendment not be entered, however, reversal of the rejection of

claims 17 and 19 under 35 USC 112, first paragraph, is submitted to be in order for the reasons that follow (it should be noted that while claims 17 and 19 are both rejected under 35 USC 112, first paragraph, the bases for the rejection of the two claims are unrelated).

The clear intent of the disclosure at page 30 is application of anti-CD44 antibodies to mucosa (vaginal, rectal or otherwise). Blood monocytes, tissue macrophage and dendritic cells are concentrated in the mucosa and it is through cells of this lineage (ie mononuclear phagocytes) that HIV is primarily transmitted. Accordingly, the subject disclosure is submitted to provide adequate written description for the term "mucosal cells" used in claim 17.

Further, page 30 of the application, last paragraph, is submitted to include a description of an "*ex vivo*" setting. That would be apparent to one skilled in the art. There is no requirement that the precise wording used in the claims (here "*ex vivo*" in claim 19) appear in the specification. Indeed, the written description provided for "*ex vivo*" is adequate to meet the requirements of 35 USC 112, first paragraph.

Reversal is requested.

The Examiner's rejections under 35 USC 112 are not well founded for the foregoing reasons and reversal of same is requested.

Respectfully submitted,

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APPENDIX

8. A method of inhibiting HIV infection of cells susceptible to HIV infection comprising contacting said cells with an amount of an agent that inhibits CD44-facilitated entry of HIV into said cells sufficient to effect said inhibition.

9. The method according to claim 8 wherein said agent is selected from the group consisting of an anti-CD44 antibody, soluble CD44, CD44 oligopeptides and hyaluronate.

11. The method according to claim 16 wherein the agent is anti-CD44 antibody A3D8 or A1G3.

13. The method according to claim 16 wherein said cell is a mononuclear phagocyte.

14. The method according to claim 13 wherein said phagocyte is a human monocyte.

15. The method according to claim 16 wherein said infection is HIV-1 infection.

16. A method of inhibiting CD44-facilitated HIV infection of a cell susceptible to HIV infection comprising contacting said cell with an amount of an anti-CD44 antibody sufficient to bind to CD44 molecules present on the surface of said cell and thereby inhibit said CD44-facilitated infection of said cell.

17. The method according to claim 13 wherein said mononuclear phagocytes are mucosal cells.

18. The method according to claim 13 wherein said contacting is effected by topical administration.

19. The method according to claim 16 wherein said cells are *ex vivo* mononuclear phagocytes.